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Table 1. Summary of the Sudden Infant Death Syndrome Cohort Demographics

Demographics		European Ancestry (n=278)
Sex	**Male**	173 (62.2%)
	Female	105 (37.8%)
Age	**Average (months)**	2.7 ± 1.98
	Range (months)	0.1 -12
Age Group	**< 2 months**	81 (29.1%)
	2 – 4 months	154 (55.4%)
	> 4 months	43 (15.5%)
Gender	**Male**	173 (62.2%)
	Female	105 (37.8%)
Sleep Position	**Supine**	85 (30.6%)
	Prone	52 (18.7%)
	Side	29 (10.4%)
	Seated	2 (0.72%)
	Unknown	110 (39.6%)
Co-sleeping	**Yes**	66 (23.7%)
	No	106 (38.1%)
	Unknown	106 (38.1%)

Table 2. Summary of 405 Genes with a Higher Prevalence (p<0.05) of Ultra-Rare, Non-Synonymous Variants in Cases Compared to Controls

Number	Gene ID	pValue	Odds Ratio (OR)	Number of Variant Positive Cases (n=278)	Number of Variant Positive Controls (n=973)
1	*LRP1*	0.00026851	3.8948	16 (5.8%)	15 (1.5%)
2	*LHX9*	0.00052687	INF	5 (1.8%)	0
3	*PDS5A*	0.00065675	21.389	6 (2.2%)	1 (0.1%)
4	*ULK1*	0.0021371	10.68	6 (2.2%)	2 (0.2%)
5	*NR3C2*	0.0021371	10.68	6 (2.2%)	2 (0.2%)
6	*OR4C6*	0.0023978	INF	4 (1.4%)	0
7	*CHRM3*	0.0023978	INF	4 (1.4%)	0
8	*CYB5D1*	0.0023978	INF	4 (1.4%)	0
9	*GBP2*	0.0023978	INF	4 (1.4%)	0
10	*ZNF506*	0.0023978	INF	4 (1.4%)	0
11	*IFRD2*	0.0023978	INF	4 (1.4%)	0
12	*BICD2*	0.0023978	INF	4 (1.4%)	0
13	*KDM4DL*	0.002584	17.751	5 (1.8%)	1 (0.1%)
14	*TNFRSF10D*	0.002584	17.751	5 (1.8%)	1 (0.1%)
15	*CTIF*	0.0035877	6.2452	7 (2.5%)	4 (0.4%)
16	*COL20A1*	0.0035877	6.2452	7 (2.5%)	4 (0.4%)
17	*ARHGEF16*	0.0045947	4.7675	8 (2.9%)	6 (0.6%)
18	*KIAA1875*	0.0051873	4.03	9 (3.2%)	8 (0.8%)
19	*CNKSR1*	0.0052208	7.1175	6 (2.2%)	3 (0.3%)
20	*ABR*	0.0052208	7.1175	6 (2.2%)	3 (0.3%)
21	*CYP11B2*	0.0052208	7.1175	6 (2.2%)	3 (0.3%)
22	*MEGF9*	0.0052208	7.1175	6 (2.2%)	3 (0.3%)
23	*AKAP13*	0.00628	2.5831	15 (5.4%)	21 (2.1%)
24	*EIF2C4*	0.0069909	4.9923	7 (2.5%)	5 (0.5%)
25	*ZMYM2*	0.0074023	8.8715	5 (1.8%)	2 (0.2%)
26	*APOBR*	0.0074023	8.8715	5 (1.8%)	2 (0.2%)
27	*SEZ6*	0.0074023	8.8715	5 (1.8%)	2 (0.2%)
28	*ALOX15*	0.0074023	8.8715	5 (1.8%)	2 (0.2%)
29	*ZNF131*	0.0074023	8.8715	5 (1.8%)	2 (0.2%)
30	*LPL*	0.0074023	8.8715	5 (1.8%)	2 (0.2%)
31	*CYP17A1*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
32	*MTHFR*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
33	*ISG20L2*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
34	*SLC22A25*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
35	*SELPLG*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
36	*PFKM*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
37	*OR6C1*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
38	*TMEM53*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
39	*EME2*	0.0098818	14.151	4 (1.4%)	1 (0.1%)

40	*CCDC55*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
41	*SUZ12*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
42	*RAB40B*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
43	*ZSCAN4*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
44	*TCP10L*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
45	*TMEM131*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
46	*MSH3*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
47	*RSPH3*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
48	*ME1*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
49	*SMURF1*	0.0098818	14.151	4 (1.4%)	1 (0.1%)
50	*CTC1*	0.01064	5.3343	6 (2.2%)	4 (0.4%)
51	*POLR1B*	0.01064	5.3343	6 (2.2%)	4 (0.4%)
52	*RTN4*	0.01064	5.3343	6 (2.2%)	4 (0.4%)
53	*CPB1*	0.01064	5.3343	6 (2.2%)	4 (0.4%)
54	*VARS*	0.01064	5.3343	6 (2.2%)	4 (0.4%)
55	*NCOA2*	0.01064	5.3343	6 (2.2%)	4 (0.4%)
56	*SORT1*	0.010882	INF	3 (1.1%)	0
57	*PITPNM1*	0.010882	INF	3 (1.1%)	0
58	*RNF121*	0.010882	INF	3 (1.1%)	0
59	*ZNF678*	0.010882	INF	3 (1.1%)	0
60	*CACNB3*	0.010882	INF	3 (1.1%)	0
61	*EIF2C1*	0.010882	INF	3 (1.1%)	0
62	*GDE1*	0.010882	INF	3 (1.1%)	0
63	*PSKH1*	0.010882	INF	3 (1.1%)	0
64	*COTL1*	0.010882	INF	3 (1.1%)	0
65	*NEGR1*	0.010882	INF	3 (1.1%)	0
66	*GSG2*	0.010882	INF	3 (1.1%)	0
67	*SCPEP1*	0.010882	INF	3 (1.1%)	0
68	*FAM73A*	0.010882	INF	3 (1.1%)	0
69	*C19orf26*	0.010882	INF	3 (1.1%)	0
70	*DUSP15*	0.010882	INF	3 (1.1%)	0
71	*TRMT6*	0.010882	INF	3 (1.1%)	0
72	*RRP7A*	0.010882	INF	3 (1.1%)	0
73	*TEX264*	0.010882	INF	3 (1.1%)	0
74	*PCBD2*	0.010882	INF	3 (1.1%)	0
75	*ERGIC1*	0.010882	INF	3 (1.1%)	0
76	*MIER3*	0.010882	INF	3 (1.1%)	0
77	*HBP1*	0.010882	INF	3 (1.1%)	0
78	*CPA1*	0.010882	INF	3 (1.1%)	0
79	*ZFP41*	0.010882	INF	3 (1.1%)	0
80	*NRBP2*	0.010882	INF	3 (1.1%)	0
81	*TRUB2*	0.010882	INF	3 (1.1%)	0
82	*KIAA0556*	0.011783	2.8191	11 (4.0)	14 (1.4%)
83	*CHIT1*	0.012308	4.1568	7 (2.5%)	6 (0.6%)
84	*SLC4A5*	0.012308	4.1568	7 (2.5%)	6 (0.6%)
85	*SEC31A*	0.012308	4.1568	7 (2.5%)	6 (0.6%)
86	*TBC1D1*	0.012927	3.5691	8 (2.9%)	8 (0.8%)
87	*PXDNL*	0.012927	3.5691	8 (2.9%)	8 (0.8%)

88	*KLHDC7A*	0.016178	5.9107	5 (1.8%)	3 (0.3%)
89	*ATG2B*	0.016178	5.9107	5 (1.8%)	3 (0.3%)
90	*THSD4*	0.016178	5.9107	5 (1.8%)	3 (0.3%)
91	*TMEM143*	0.016178	5.9107	5 (1.8%)	3 (0.3%)
92	*RRP1B*	0.016178	5.9107	5 (1.8%)	3 (0.3%)
93	*VPS8*	0.016178	5.9107	5 (1.8%)	3 (0.3%)
94	*C4orf41*	0.016178	5.9107	5 (1.8%)	3 (0.3%)
95	*PCDHA4*	0.016178	5.9107	5 (1.8%)	3 (0.3%)
96	*SH2D4A*	0.016178	5.9107	5 (1.8%)	3 (0.3%)
97	*FANCC*	0.016178	5.9107	5 (1.8%)	3 (0.3%)
98	*PEX5*	0.019102	4.2641	6 (2.2%)	5 (0.5%)
99	*NYNRIN*	0.019102	4.2641	6 (2.2%)	5 (0.5%)
100	*PTPRM*	0.019102	4.2641	6 (2.2%)	5 (0.5%)
101	*PLD1*	0.019102	4.2641	6 (2.2%)	5 (0.5%)
102	*FAM193A*	0.019102	4.2641	6 (2.2%)	5 (0.5%)
103	*KIAA1731*	0.019807	3.1699	8 (2.9%)	9 (0.9%)
104	*KDM6B*	0.019807	3.1699	8 (2.9%)	9 (0.9%)
105	*PRR14L*	0.019807	3.1699	8 (2.9%)	9 (0.9%)
106	*CPSF1*	0.019807	3.1699	8 (2.9%)	9 (0.9%)
107	*RNF111*	0.020022	3.5597	7 (2.5%)	7 (0.7%)
108	*TGS1*	0.020022	3.5597	7 (2.5%)	7 (0.7%)
109	*MUC17*	0.023956	2.076	15 (5.4)	26 (2.6%)
110	*KIAA1279*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
111	*WDR47*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
112	*ANKK1*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
113	*AP4B1*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
114	*SMTNL1*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
115	*CD247*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
116	*RBMXL2*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
117	*SETD1B*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
118	*PIWIL1*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
119	*ATN1*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
120	*HECTD3*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
121	*RIN3*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
122	*DAPK2*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
123	*C15orf58*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
124	*PLCG1*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
125	*HIC2*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
126	*MTMR14*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
127	*KLF3*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
128	*AC104650.1*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
129	*NUP155*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
130	*ADAMTS6*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
131	*ZNF618*	0.024477	7.0729	4 (1.4%)	2 (0.2%)
132	*SPTBN5*	0.026701	2.2634	12 (4.3)	19 (1.9%)
133	*SDK2*	0.028944	2.8502	8 (2.9%)	10 (1.0%)
134	*SART1*	0.029874	4.4299	5 (1.8%)	4 (0.4%)
135	*SLC29A2*	0.029874	4.4299	5 (1.8%)	4 (0.4%)

136	*FAM161B*	0.029874	4.4299	5 (1.8%)	4 (0.4%)
137	*NUP85*	0.029874	4.4299	5 (1.8%)	4 (0.4%)
138	*LRRN1*	0.029874	4.4299	5 (1.8%)	4 (0.4%)
139	*PIGG*	0.029874	4.4299	5 (1.8%)	4 (0.4%)
140	*HELQ*	0.029874	4.4299	5 (1.8%)	4 (0.4%)
141	*UGT3A1*	0.029874	4.4299	5 (1.8%)	4 (0.4%)
142	*ABCA3*	0.030564	3.1122	7 (2.5%)	8 (0.8%)
143	*FN1*	0.030564	3.1122	7 (2.5%)	8 (0.8%)
144	*AKAP12*	0.030564	3.1122	7 (2.5%)	8 (0.8%)
145	*KCNH5*	0.031213	3.5503	6 (2.2%)	6 (0.6%)
146	*NLRP11*	0.031213	3.5503	6 (2.2%)	6 (0.6%)
147	*TKTL2*	0.031213	3.5503	6 (2.2%)	6 (0.6%)
148	*PCDHGB1*	0.031213	3.5503	6 (2.2%)	6 (0.6%)
149	*HPSE2*	0.036334	10.575	3 (1.1%)	1 (0.1%)
150	*MPP7*	0.036334	10.575	3 (1.1%)	1 (0.1%)
151	*C11orf92*	0.036334	10.575	3 (1.1%)	1 (0.1%)
152	*PANX3*	0.036334	10.575	3 (1.1%)	1 (0.1%)
153	*LDHC*	0.036334	10.575	3 (1.1%)	1 (0.1%)
154	*OR52R1*	0.036334	10.575	3 (1.1%)	1 (0.1%)
155	*APLNR*	0.036334	10.575	3 (1.1%)	1 (0.1%)
156	*RNPEP*	0.036334	10.575	3 (1.1%)	1 (0.1%)
157	*PPP1R12A*	0.036334	10.575	3 (1.1%)	1 (0.1%)
158	*NUFIP1*	0.036334	10.575	3 (1.1%)	1 (0.1%)
159	*HSP90AA1*	0.036334	10.575	3 (1.1%)	1 (0.1%)
160	*OR4E2*	0.036334	10.575	3 (1.1%)	1 (0.1%)
161	*LTB4R*	0.036334	10.575	3 (1.1%)	1 (0.1%)
162	*DPH2*	0.036334	10.575	3 (1.1%)	1 (0.1%)
163	*OTUD7A*	0.036334	10.575	3 (1.1%)	1 (0.1%)
164	*AC090651.1*	0.036334	10.575	3 (1.1%)	1 (0.1%)
165	*GCOM1*	0.036334	10.575	3 (1.1%)	1 (0.1%)
166	*PARP16*	0.036334	10.575	3 (1.1%)	1 (0.1%)
167	*HAPLN3*	0.036334	10.575	3 (1.1%)	1 (0.1%)
168	*NOMO2*	0.036334	10.575	3 (1.1%)	1 (0.1%)
169	*GLYR1*	0.036334	10.575	3 (1.1%)	1 (0.1%)
170	*SF3B3*	0.036334	10.575	3 (1.1%)	1 (0.1%)
171	*DHRS7B*	0.036334	10.575	3 (1.1%)	1 (0.1%)
172	*ETV4*	0.036334	10.575	3 (1.1%)	1 (0.1%)
173	*SLC16A5*	0.036334	10.575	3 (1.1%)	1 (0.1%)
174	*FAM69C*	0.036334	10.575	3 (1.1%)	1 (0.1%)
175	*IL12RB1*	0.036334	10.575	3 (1.1%)	1 (0.1%)
176	*S1PR4*	0.036334	10.575	3 (1.1%)	1 (0.1%)
177	*ACPT*	0.036334	10.575	3 (1.1%)	1 (0.1%)
178	*IGLON5*	0.036334	10.575	3 (1.1%)	1 (0.1%)
179	*ZNF561*	0.036334	10.575	3 (1.1%)	1 (0.1%)
180	*CPXM1*	0.036334	10.575	3 (1.1%)	1 (0.1%)
181	*SP140*	0.036334	10.575	3 (1.1%)	1 (0.1%)
182	*SP100*	0.036334	10.575	3 (1.1%)	1 (0.1%)
183	*PHF21B*	0.036334	10.575	3 (1.1%)	1 (0.1%)

184	*PROM2*	0.036334	10.575	3 (1.1%)	1 (0.1%)
185	*CEP63*	0.036334	10.575	3 (1.1%)	1 (0.1%)
186	*AADACL2*	0.036334	10.575	3 (1.1%)	1 (0.1%)
187	*MFSD1*	0.036334	10.575	3 (1.1%)	1 (0.1%)
188	*MYD88*	0.036334	10.575	3 (1.1%)	1 (0.1%)
189	*CYB561D2*	0.036334	10.575	3 (1.1%)	1 (0.1%)
190	*OR5AC2*	0.036334	10.575	3 (1.1%)	1 (0.1%)
191	*NFXL1*	0.036334	10.575	3 (1.1%)	1 (0.1%)
192	*AASDH*	0.036334	10.575	3 (1.1%)	1 (0.1%)
193	*CDKL2*	0.036334	10.575	3 (1.1%)	1 (0.1%)
194	*BTNL9*	0.036334	10.575	3 (1.1%)	1 (0.1%)
195	*LACE1*	0.036334	10.575	3 (1.1%)	1 (0.1%)
196	*SNX9*	0.036334	10.575	3 (1.1%)	1 (0.1%)
197	*SLC17A1*	0.036334	10.575	3 (1.1%)	1 (0.1%)
198	*SLC17A3*	0.036334	10.575	3 (1.1%)	1 (0.1%)
199	*KIAA1009*	0.036334	10.575	3 (1.1%)	1 (0.1%)
200	*SERPINE1*	0.036334	10.575	3 (1.1%)	1 (0.1%)
201	*MLXIPL*	0.036334	10.575	3 (1.1%)	1 (0.1%)
202	*ABHD11*	0.036334	10.575	3 (1.1%)	1 (0.1%)
203	*HTRA4*	0.036334	10.575	3 (1.1%)	1 (0.1%)
204	*PHF19*	0.036334	10.575	3 (1.1%)	1 (0.1%)
205	*STRBP*	0.036334	10.575	3 (1.1%)	1 (0.1%)
206	*NR5A1*	0.036334	10.575	3 (1.1%)	1 (0.1%)
207	*FAM69B*	0.036334	10.575	3 (1.1%)	1 (0.1%)
208	*VPS13A*	0.036334	10.575	3 (1.1%)	1 (0.1%)
209	*ZNF469*	0.038845	2.1842	11 (4.0)	18 (1.8%)
210	*ZFHX4*	0.04373	2.2301	10 (3.6)	16 (1.6%)
211	*MYO1E*	0.044281	2.7639	7 (2.5%)	9 (0.9%)
212	*DIDO1*	0.044281	2.7639	7 (2.5%)	9 (0.9%)
213	*ATP10B*	0.044281	2.7639	7 (2.5%)	9 (0.9%)
214	*CTTNBP2NL*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
215	*TSSC4*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
216	*ASPM*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
217	*NT5DC3*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
218	*TRPV4*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
219	*PAFAH2*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
220	*C1orf94*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
221	*IPP*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
222	*DOC2A*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
223	*CHST5*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
224	*ADAT1*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
225	*RAPGEFL1*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
226	*MAP2K6*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
227	*ZNF763*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
228	*TNPO2*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
229	*CC2D1A*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
230	*PNKP*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
231	*ZNF544*	0.047244	4.7125	4 (1.4%)	3 (0.3%)

232	*TM9SF4*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
233	*DNMT3B*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
234	*KRTAP10-12*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
235	*ZNF804A*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
236	*IL17RA*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
237	*RASGRP3*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
238	*INTU*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
239	*SEC24A*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
240	*AC008661.1*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
241	*TRPC7*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
242	*PCDHGA12*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
243	*PHIP*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
244	*ANKRD6*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
245	*RBM33*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
246	*CALN1*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
247	*ELN*	0.047244	4.7125	4 (1.4%)	3 (0.3%)
248	*RBP3*	0.047417	3.0407	6 (2.2%)	7 (0.7%)
249	*FARP1*	0.047417	3.0407	6 (2.2%)	7 (0.7%)
250	*GREB1L*	0.047417	3.0407	6 (2.2%)	7 (0.7%)
251	*MOV10L1*	0.047417	3.0407	6 (2.2%)	7 (0.7%)
252	*FRMD4B*	0.047417	3.0407	6 (2.2%)	7 (0.7%)
253	*ADAMTS14*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
254	*NCAPD3*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
255	*CGN*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
256	*CNTN1*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
257	*LTA4H*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
258	*SH3D21*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
259	*ZNF785*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
260	*ABCA9*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
261	*SERPINB8*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
262	*MYO1F*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
263	*MMP9*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
264	*NRIP1*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
265	*AOX1*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
266	*GIGYF2*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
267	*YTHDC2*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
268	*HSPA4*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
269	*DMGDH*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
270	*GPR116*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
271	*KIAA0368*	0.049108	3.5409	5 (1.8%)	5 (0.5%)
272	*AKAP9*	0.049138	2.29	9 (3.2%)	14 (1.4%)
273	*SMC3*	0.049244	INF	2 (0.7%)	0
274	*SHOC2*	0.049244	INF	2 (0.7%)	0
275	*PSTK*	0.049244	INF	2 (0.7%)	0
276	*FRMD4A*	0.049244	INF	2 (0.7%)	0
277	*ZNF22*	0.049244	INF	2 (0.7%)	0
278	*PAPSS2*	0.049244	INF	2 (0.7%)	0
279	*CASP1*	0.049244	INF	2 (0.7%)	0

280	*ADAMTS8*	0.049244	INF	2 (0.7%)	0
281	*FCGR1B*	0.049244	INF	2 (0.7%)	0
282	*TDRKH*	0.049244	INF	2 (0.7%)	0
283	*RORC*	0.049244	INF	2 (0.7%)	0
284	*TRIM46*	0.049244	INF	2 (0.7%)	0
285	*CCT3*	0.049244	INF	2 (0.7%)	0
286	*OR5B2*	0.049244	INF	2 (0.7%)	0
287	*CRP*	0.049244	INF	2 (0.7%)	0
288	*CCDC86*	0.049244	INF	2 (0.7%)	0
289	*SCGB2A1*	0.049244	INF	2 (0.7%)	0
290	*KCNK4*	0.049244	INF	2 (0.7%)	0
291	*C11orf24*	0.049244	INF	2 (0.7%)	0
292	*P2RY2*	0.049244	INF	2 (0.7%)	0
293	*OLFML1*	0.049244	INF	2 (0.7%)	0
294	*RGS1*	0.049244	INF	2 (0.7%)	0
295	*KLRC2*	0.049244	INF	2 (0.7%)	0
296	*RP11-277P12.6*	0.049244	INF	2 (0.7%)	0
297	*C12orf24*	0.049244	INF	2 (0.7%)	0
298	*SLC30A1*	0.049244	INF	2 (0.7%)	0
299	*IFLTD1*	0.049244	INF	2 (0.7%)	0
300	*PTHLH*	0.049244	INF	2 (0.7%)	0
301	*AMN1*	0.049244	INF	2 (0.7%)	0
302	*SLC6A13*	0.049244	INF	2 (0.7%)	0
303	*TRIM58*	0.049244	INF	2 (0.7%)	0
304	*ARF3*	0.049244	INF	2 (0.7%)	0
305	*C12orf44*	0.049244	INF	2 (0.7%)	0
306	*TBK1*	0.049244	INF	2 (0.7%)	0
307	*TFDP1*	0.049244	INF	2 (0.7%)	0
308	*SCEL*	0.049244	INF	2 (0.7%)	0
309	*MFSD2A*	0.049244	INF	2 (0.7%)	0
310	*EDDM3B*	0.049244	INF	2 (0.7%)	0
311	*SLC39A2*	0.049244	INF	2 (0.7%)	0
312	*PPP2R3C*	0.049244	INF	2 (0.7%)	0
313	*ENTPD5*	0.049244	INF	2 (0.7%)	0
314	*ISM2*	0.049244	INF	2 (0.7%)	0
315	*TCL1B*	0.049244	INF	2 (0.7%)	0
316	*AVEN*	0.049244	INF	2 (0.7%)	0
317	*JMJD7-PLA2G4B*	0.049244	INF	2 (0.7%)	0
318	*MAP2K5*	0.049244	INF	2 (0.7%)	0
319	*CLN6*	0.049244	INF	2 (0.7%)	0
320	*MORF4L1*	0.049244	INF	2 (0.7%)	0
321	*HES3*	0.049244	INF	2 (0.7%)	0
322	*ANKS3*	0.049244	INF	2 (0.7%)	0
323	*TERF2*	0.049244	INF	2 (0.7%)	0
324	*TP53I13*	0.049244	INF	2 (0.7%)	0
325	*MSL1*	0.049244	INF	2 (0.7%)	0
326	*CNP*	0.049244	INF	2 (0.7%)	0
327	*KCNJ2*	0.049244	INF	2 (0.7%)	0

328	*NXN*	0.049244	INF	2 (0.7%)	0
329	*SOX15*	0.049244	INF	2 (0.7%)	0
330	*PYCR1*	0.049244	INF	2 (0.7%)	0
331	*SLC25A35*	0.049244	INF	2 (0.7%)	0
332	*ELTD1*	0.049244	INF	2 (0.7%)	0
333	*PIAS2*	0.049244	INF	2 (0.7%)	0
334	*FBXO15*	0.049244	INF	2 (0.7%)	0
335	*VAPA*	0.049244	INF	2 (0.7%)	0
336	*ZNF326*	0.049244	INF	2 (0.7%)	0
337	*CNN1*	0.049244	INF	2 (0.7%)	0
338	*GAMT*	0.049244	INF	2 (0.7%)	0
339	*TECR*	0.049244	INF	2 (0.7%)	0
340	*AP1M1*	0.049244	INF	2 (0.7%)	0
341	*LGALS14*	0.049244	INF	2 (0.7%)	0
342	*NTN5*	0.049244	INF	2 (0.7%)	0
343	*HSD11B1L*	0.049244	INF	2 (0.7%)	0
344	*ZIM3*	0.049244	INF	2 (0.7%)	0
345	*CENPB*	0.049244	INF	2 (0.7%)	0
346	*SRSF6*	0.049244	INF	2 (0.7%)	0
347	*TNFRSF6B*	0.049244	INF	2 (0.7%)	0
348	*C21orf91*	0.049244	INF	2 (0.7%)	0
349	*MRPL39*	0.049244	INF	2 (0.7%)	0
350	*TNFAIP6*	0.049244	INF	2 (0.7%)	0
351	*HOXD1*	0.049244	INF	2 (0.7%)	0
352	*SGOL2*	0.049244	INF	2 (0.7%)	0
353	*SCG2*	0.049244	INF	2 (0.7%)	0
354	*TIMP3*	0.049244	INF	2 (0.7%)	0
355	*AQP12B*	0.049244	INF	2 (0.7%)	0
356	*NRBP1*	0.049244	INF	2 (0.7%)	0
357	*HHLA2*	0.049244	INF	2 (0.7%)	0
358	*MORC1*	0.049244	INF	2 (0.7%)	0
359	*ABHD10*	0.049244	INF	2 (0.7%)	0
360	*CD200*	0.049244	INF	2 (0.7%)	0
361	*ZNF639*	0.049244	INF	2 (0.7%)	0
362	*AC022498.1*	0.049244	INF	2 (0.7%)	0
363	*ZDHHC19*	0.049244	INF	2 (0.7%)	0
364	*FHIT*	0.049244	INF	2 (0.7%)	0
365	*SNTN*	0.049244	INF	2 (0.7%)	0
366	*ARL6IP5*	0.049244	INF	2 (0.7%)	0
367	*TTC29*	0.049244	INF	2 (0.7%)	0
368	*STOX2*	0.049244	INF	2 (0.7%)	0
369	*KCNIP4*	0.049244	INF	2 (0.7%)	0
370	*TMPRSS11BNL*	0.049244	INF	2 (0.7%)	0
371	*CXCL6*	0.049244	INF	2 (0.7%)	0
372	*ROPN1L*	0.049244	INF	2 (0.7%)	0
373	*DAP*	0.049244	INF	2 (0.7%)	0
374	*RELL2*	0.049244	INF	2 (0.7%)	0
375	*NOP16*	0.049244	INF	2 (0.7%)	0

376	*RAD1*	0.049244	INF	2 (0.7%)	0
377	*LMBRD2*	0.049244	INF	2 (0.7%)	0
378	*GZMA*	0.049244	INF	2 (0.7%)	0
379	*SREK1*	0.049244	INF	2 (0.7%)	0
380	*TAS2R1*	0.049244	INF	2 (0.7%)	0
381	*C6orf52*	0.049244	INF	2 (0.7%)	0
382	*NRSN1*	0.049244	INF	2 (0.7%)	0
383	*HIST1H2AE*	0.049244	INF	2 (0.7%)	0
384	*DAXX*	0.049244	INF	2 (0.7%)	0
385	*RRP36*	0.049244	INF	2 (0.7%)	0
386	*CRISP3*	0.049244	INF	2 (0.7%)	0
387	*LY86*	0.049244	INF	2 (0.7%)	0
388	*WNT2*	0.049244	INF	2 (0.7%)	0
389	*OPN1SW*	0.049244	INF	2 (0.7%)	0
390	*STRA8*	0.049244	INF	2 (0.7%)	0
391	*GIMAP8*	0.049244	INF	2 (0.7%)	0
392	*TAX1BP1*	0.049244	INF	2 (0.7%)	0
393	*STX1A*	0.049244	INF	2 (0.7%)	0
394	*SGCE*	0.049244	INF	2 (0.7%)	0
395	*CYP3A5*	0.049244	INF	2 (0.7%)	0
396	*DEFB135*	0.049244	INF	2 (0.7%)	0
397	*EFHA2*	0.049244	INF	2 (0.7%)	0
398	*ADRA1A*	0.049244	INF	2 (0.7%)	0
399	*CRISPLD1*	0.049244	INF	2 (0.7%)	0
400	*DPY19L4*	0.049244	INF	2 (0.7%)	0
401	*MRPL50*	0.049244	INF	2 (0.7%)	0
402	*C9orf150*	0.049244	INF	2 (0.7%)	0
403	*C9orf78*	0.049244	INF	2 (0.7%)	0
404	*GALT*	0.049244	INF	2 (0.7%)	0
405	*CDC37L1*	0.049244	INF	2 (0.7%)	0

INF = infinite

Table 2. Summary of Genes with an Over-Representation of Ultra-Rare Variants with a MAF < 0.00005

Gene ID	Gene/Protein Name	pValue	Odds Ratio (OR)	Number of Variant Positive Cases (n=278)	Number of Variant Positive Controls (n=973)
LRP1	LDL Receptor Related Protein 1	0.000269	3.8948	16 (5.8%)	15 (1.5%)
LHX9	LIM Homeobox 9	0.000527	INF	5 (1.8%)	0
PDS5A	PDS5 Cohesin Associated Factor A	0.000657	21.389	6 (2.2%)	1 (0.1%)
ULK1	Unc-51 Like Autophagy Activating Kinase 1	0.002137	10.68	6 (2.2%)	2 (0.21%)
NR3C2	Nuclear Receptor Subfamily 3 Group C Member 2	0.002137	10.68	6 (2.2%)	2 (0.21%)
OR4C6	Olfactory Receptor Family 4 Subfamily C Member 6	0.002398	INF	4 (1.4%)	0
CHRM3	Cholinergic Receptor Muscarinic 3	0.002398	INF	4 (1.4%)	0
CYB5D1	Cytochrome B5 Domain Containing 1	0.002398	INF	4 (1.4%)	0
GBP2	Guanylate Binding Protein 2	0.002398	INF	4 (1.4%)	0
ZNF506	Zinc Finger Protein 506	0.002398	INF	4 (1.4%)	0
IFRD2	Interferon-Related Developmental Regulator 2	0.002398	INF	4 (1.4%)	0
BICD2	BICD Cargo Adaptor 2	0.002398	INF	4 (1.4%)	0
KDM4DL	Lysine Demethylase 4E	0.002584	17.751	5 (1.8%)	1 (0.1%)
TNFRSF10D	Tumor Necrosis Factor Receptor Superfamily Member 10d	0.002584	17.751	5 (1.8%)	1 (0.1%)
CTIF	CBP80/20-Dependent Translation Initiation Factor	0.003588	6.2452	7 (2.5%)	4 (0.4%)
COL20A1	Collagen Type XX Alpha 1	0.003588	6.2452	7 (2.5%)	4 (0.4%)
ARHGEF16	Rho Guanine Nucleotide Exchange Factor 16	0.004595	4.7675	8 (2.9%)	6 (0.62%)

Genes are listed in ascending order by their p-value. INF = infinite.

Table 4. Summary of Genes with an Over-Representation of Ultra-Rare Variants with a MAF < 0.00005

Gene ID	Gene/Protein Name	OMIM Disease Associations	PathCards SuperPathways	pValue	Odds Ratio (OR)	Number of Variant Positive Cases (n=278)	Number of Variant Positive Controls (n=973)
LRP1	LDL Receptor Related Protein 1	1) Association with Alzheimer disease 2) Association with Abdominal Aortic Aneurysm 3) Intellectual Disability	1) Statin Pathway 2) A-beta Pathways: Uptake and Degradation 3) Alzheimers Disease Pathway 4) Malaria 5) PDGFR-beta signaling pathway 6) amb2 Integrin signaling 7) Binding and Uptake of Ligands by Scavenger Receptors 8) Blood-Brain Barrier and Immune Cell Transmigration: Pathways Overview 9) Metabolism of fat-soluble vitamins 10) Non-Canonical Wnt Pathway 11) Metabolism of water-soluble vitamins and cofactors 12) Wnt signaling pathway (KEGG) 13) Alzheimer's disease 14) Vesicle-mediated transport 15) Signaling by GPCR 16) Metabolism	0.000269	3.8948	16 (5.8%)	15 (1.5%)
LHX9	LIM Homeobox 9	None	None	0.000527	INF	5 (1.8%)	0
PDS5A	PDS5 Cohesin Associated Factor A	None	None	0.000657	21.389	6 (2.2%)	1 (0.1%)

ULK1	Unc-51 Like Autophagy Activating Kinase 1	None	1) Regulation of autophagy 2) Senescence and Autophagy 3) Longevity regulating pathway - multiple species 4) AMPK signaling pathway 5) p53 Pathway (RnD) 6) mTOR signalling 7) Glucose / Energy Metabolism 8) Neuroscience 9) Translation Insulin regulation of translation 10) Cellular Senescence	0.002137	10.68	6 (2.2%)	2 (0.21%)
NR3C2	Nuclear Receptor Subfamily 3 Group C Member 2	1) Pseudohypoaldosteronism Type I, Autosomal Dominant 2) Hypertension, Early-Onset, Autosomal Dominant, with Severe Exacerbation in Pregnancy	1) Aldosterone-regulated sodium reabsorption 2) Agents Acting on the Renin-Angiotensin System Pathway, Pharmacodynamics 3) Nuclear Receptor transcription pathway 4) Gene Expression	0.002137	10.68	6 (2.2%)	2 (0.21%)
OR4C6	Olfactory Receptor Family 4 Subfamily C Member 6	None	1) Olfactory Signaling Pathway 2) Signaling by GPCR	0.002398	INF	4 (1.4%)	0

CHRM3	Cholinergic Receptor Muscarinic 3	1) Purne Belly Syndrome (autosomal recessive)	1) Proton Pump Inhibitor Pathway, Pharmacodynamics 2) Monoamine GPCRs 3) GPCRs, Other 4) Taste transduction 5) Pancreatic secretion 6) Integration of energy metabolism 7) Salivary secretion 8) Insulin secretion 9) Myometrial Relaxation and Contraction Pathways 10) Calcium signaling pathway 11) Regulation of actin cytoskeleton 12) Circadian entrainment 13) Peptide ligand-binding receptors 14) Interleukin-3, 5 and GM-CSF signaling 15) Signaling by GPCR 16) Metabolism	0.002398	INF	4 (1.4%)	0
CYB5D1	Cytochrome B5 Domain Containing 1	None	None	0.002398	INF	4 (1.4%)	0
GBP2	Guanylate Binding Protein 2	None	1) Immune response IFN alpha/beta signaling pathway 2) Interferon gamma signaling 3) Interleukin-3, 5 and GM-CSF signaling 4) Immune System	0.002398	INF	4 (1.4%)	0
ZNF506	Zinc Finger Protein 506	None	1) Gene Expression	0.002398	INF	4 (1.4%)	0
IFRD2	Interferon-Related Developmental Regulator 2	None	None	0.002398	INF	4 (1.4%)	0
BICD2	BICD Cargo Adaptor 2	1) Autosomal dominant lower extremity-predominant spinal muscular atrophy-2	1) COPI-independent Golgi-to-ER retrograde traffic 2) Golgi-to-ER retrograde transport 3) Vesicle-mediated transport	0.002398	INF	4 (1.4%)	0
KDM4DL	Lysine Demethylase 4E	None	None	0.002584	17.751	5 (1.8%)	1 (0.1%)

TNFRSF10D	Tumor Necrosis Factor Receptor Superfamily Member 10d	None	None	0.002584	17.751	5 (1.8%)	1 (0.1%)
CTIF	CBP80/20-Dependent Translation Initiation Factor	None	None	0.003588	6.2452	7 (2.5%)	4 (0.4%)
COL20A1	Collagen Type XX Alpha 1	None	1) Collagen biosynthesis and modifying enzymes 2) Degradation of the extracellular matrix 3) Integrin Pathway 4) Phospholipase-C Pathway 5) ERK Signaling	0.003588	6.2452	7 (2.5%)	4 (0.4%)
ARHGEF16	Rho Guanine Nucleotide Exchange Factor 16	None	1) NgR-p75(NTR)-Mediated Signaling 2) Signaling by Slit 3) Interferon Pathway 4) p75 NTR receptor-mediated signalling 5) Guidance Cues and Growth Cone Motility 6) G-AlphaQ Signaling 7) RhoGDI Pathway 8) fMLP Pathway 9) Actin Nucleation by ARP-WASP Complex 10) Signaling by Rho GTPases 11) TGF-Beta Pathway 12) Phospholipase-C Pathway 13) GPCR Pathway 14) Apoptotic Pathways in Synovial Fibroblasts 15) Interleukin-3, 5 and GM-CSF signaling 16) ERK Signaling 17) Signaling by GPCR	0.004595	4.7675	8 (2.9%)	6 (0.62%)

INF = infinite

Table 5. Summary of Genes with an Over-Representation of Ultra-Rare Variants with a MAF < 0.00005 and a CADD Score > 20

Gene ID	Gene/Protein Name	OMIM Disease Associations	PathCards SuperPathways	pValue	Odds Ratio (OR)	Number of Variant Positive Cases (n=278)	Number of Variant Positive Controls (n=973)
PTPRM	Protein Tyrosine Phosphatase, Receptor Type M	None	1) Nectin adhesion pathway 2) Cell adhesion_Cadherin-mediated cell adhesion 3) Adherens junction 4) Adhesion 5) Cell adhesion molecules (CAMs) 6) PAK Pathway	0.000657	21.389	6 (2.2%)	1 (0.1%)
CNKSR1	Connector Enhancer Of Kinase Suppressor Of Ras 1	None	1) MAP2K and MAPK activation 2) Ceramide Pathway 3) Toll-Like receptor Signaling Pathways 4) ERK Signaling 5) Developmental Biology 6) Interleukin-3, 5 and GM-CSF signaling 7) Immune System 8) Signaling by GPCR	0.002137	10.68	6 (2.2%)	2 (0.21%)
KDM6B	Lysine Demethylase 6B	None	1) Chromatin Regulation / Acetylation 2) Chromatin organization 3) Cellular Senescence 4) Activated PKN1 stimulates transcription of AR (androgen receptor) regulated genes KLK2 and KLK3	0.002137	10.68	6 (2.2%)	2 (0.21%)
NR3C2	Nuclear Receptor Subfamily 3 Group C Member 2	1)Pseudohypoaldosteronism Type I, Autosomal Dominant 2) Hypertension, Early-Onset, Autosomal Dominant, with Severe Exacerbation in Pregnancy	1) Aldosterone-regulated sodium reabsorption 2) Agents Acting on the Renin-Angiotensin System Pathway, Pharmacodynamics 3) Nuclear Receptor transcription pathway 4) Gene Expression	0.002137	10.68	6 (2.2%)	2 (0.21%)

ABCA2	ATP Binding Cassette Subfamily A Member 2	1) Alzheimer Disease	1) ABC-family proteins mediated transport 2) Lysosome 3) Transport of glucose and other sugars, bile salts and organic acids, metal ions and amine compounds	0.002137	10.68	6 (2.2%)	2 (0.21%)
LHX9	LIM Homeobox 9	None	None	0.002398	INF	4 (1.4%)	0
ABR	Active BCR-Related	none	1) G-protein signaling_Rac2 regulation pathway 2) Regulation of RAC1 activity 3) G-protein signaling_Regulation of CDC42 activity 4) G-protein signaling_Regulation of RAC1 activity 5) Regulation of RhoA activity 6) p75 NTR receptor-mediated signalling 7) Signaling by Rho GTPases 8) Interleukin-3, 5 and GM-CSF signaling 9) Signaling by GPCR	0.002398	INF	4 (1.4%)	0
ERGIC1	Endoplasmic Reticulum-Golgi Intermediate Compartment 1	None	None	0.002398	INF	4 (1.4%)	0
DMGDH	Dimethylglycine Dehydrogenase	1) Dimethylglycine Dehydrogenase Deficiency Inborn Error of Metabolism	1) Glycine, serine and threonine metabolism 2) Glycerophospholipid biosynthesis 3) Metabolism	0.002584	17.751	5 (1.8%)	1 (0.1%)

Table 3. Ingenuity® Pathway Analysis – Top Canonical Pathway Genes

Pathway	IPA derived pathway level pValue	IPA Overlap (%)	Gene Symbol	Entrez Gene Name	pValue	Odds Ratio (OR)	Number of Variant Positive Cases (n=278)	Number of Variant Positive Controls (n=973)
Glucocorticoid Biosynthesis	0.0107	2/8 (25)	*CYP11B2*	cytochrome P450 family 11 subfamily B member 2	0.005221	7.1175	6 (2.2%)	3 (0.3%)
			CYP17A1	cytochrome P450 family 17 subfamily A member 1	0.009882	14.151	4 (1.4%)	1 (0.1%)
Melatonin Signaling	0.0133	5/69 (7.2%)	*MAP2K5*	mitogen-activated protein kinase kinase 5	0.049244	INF	2 (0.7%)	0
			MAP2K6	mitogen-activated protein kinase kinase 6	0.047244	4.7125	4 (1.4%)	3 (0.3%)
			OPN1SW	opsin 1 (cone pigments), short-wave-sensitive	0.049244	INF	2 (0.7%)	0
			PLCG1	phospholipase C gamma 1	0.024477	7.0729	4 (1.4%)	2 (0.2%)
			RORC	RAR related orphan receptor C	0.049244	INF	2 (0.7%)	0
Role of IL-17A in Psoriasis	0.0279	2/13 (15.4%)	*CXCL6*	C-X-C motif chemokine ligand 6	0.049244	INF	2 (0.7%)	0
			IL17RA	interleukin 17 receptor A	0.047244	4.7125	4 (1.4%)	3 (0.3%)
Sulfate Activation for Sulfonation	0.0404	1/2 (50%)	*PAPSS2*	3'-phosphoadenosine 5'-phosphosulfate synthase 2	0.049244	INF	2 (0.7%)	0
Glycine Degradation (Creatine Biosynthesis)	0.0404	1/2 (50%)	*GAMT*	guanidinoacetate N-methyltransferase	0.049244	INF	2 (0.7%)	0

INF=infinite